

WHAT IS CLAIMED IS:

1. A method of producing a population of antigen-specific immune cells in a mammal comprising:
  - contacting a hematopoietic stem cell with a polynucleotide delivery system comprising an antigen specific polynucleotide; and
  - transferring the hematopoietic stem cell into the mammal,
  - wherein the antigen-specific polynucleotide encodes the  $\alpha$  and  $\beta$  subunits of a T cell receptor.
2. The method of claim 1 wherein the hematopoietic stem cell is contacted with the polynucleotide delivery system ex vivo.
3. The method of claim 1, wherein the hematopoietic stem cell is a primary bone marrow cell.
4. The method of claim 1 wherein the immune cells are T cells.
5. The method of claim 1 wherein an IRES element is disposed between the  $\alpha$  and  $\beta$  subunits.
6. The method of claim 1 wherein the polynucleotide delivery system comprises a single promoter operably linked to the antigen specific polynucleotide.
7. The method of claim 1 wherein the polynucleotide delivery system comprises a modified retrovirus.
8. The method of claim 7 wherein the polynucleotide delivery system comprises a modified lentivirus.
9. The method of claim 1 wherein the polynucleotide delivery system further comprises a gene that enhances immune cell function.
10. The method of claim 9 wherein the gene and the antigen-specific polypeptide are operably linked to a single promoter.
11. The method of claim 9 wherein the gene encodes an immunomodulatory protein.
12. The method of claim 11 wherein the immunomodulatory protein is the IL2 receptor CD25.
13. The method of claim 9 wherein the gene encodes a cytokine.

14. The method of claim 13 wherein the cytokine is selected from the group consisting of IL-2, IL-4 and IFN-r.
15. The method of claim 9 wherein the gene encodes a cytokine receptor.
16. The method of claim 15 wherein the cytokine receptor is selected from the group consisting of IL-2R, CD25, IL-4R, IL-7R and IL-15R.
17. The method of claim 1 wherein the hematopoietic stem cell is obtained from the mammal in which the immune cell is to be generated.
18. The method of claim 1 wherein transferring the hematopoietic stem cell into the mammal comprises injection into the peripheral blood.
19. A method of treating cancer in a patient comprising:
  - identifying an antigen associated with the cancer;
  - obtaining a polynucleotide that encodes a T cell receptor that specifically binds the antigen;
  - contacting hematopoietic stem cells with a polynucleotide delivery system comprising the polynucleotide; and
  - transferring the stem cells into the patient.
20. The method of claim 19 wherein the hematopoietic stem cells are obtained from the patient prior to being contacted with the polynucleotide delivery system.
21. The method of claim 19 wherein the hematopoietic stem cells are primary bone marrow cells.
22. The method of claim 19 wherein the polynucleotide delivery system is a modified retrovirus.
23. The method of claim 22 wherein the modified retrovirus is a modified lentivirus.
24. The method of claim 19 wherein the polynucleotide encodes a T cell receptor  $\alpha$  subunit and a T cell receptor  $\beta$  subunit.
25. The method of claim 24 wherein the polynucleotide delivery system comprises an IRES element disposed between the  $\alpha$  subunit and the  $\beta$  subunit.
26. The method of claim 19 additionally comprising injecting the patient with purified antigen.
27. A method of treating melanoma in a patient comprising:

contacting hematopoietic stem cells with a polynucleotide delivery system comprising cDNA encoding a T cell receptor that is specific for a melanoma antigen; and

transferring the stem cells into the patient.

28. The method of claim 27 wherein the cDNA encodes a T cell receptor that is specific for an epitope of Mart-1.

29. The method of claim 28 wherein the polynucleotide delivery system comprises the nucleic acid sequence of SEQ ID NO: 2.

30. The method of claim 27 wherein the cDNA encodes a T cell receptor that is specific for an epitope of gp-100.

31. The method of claim 30 wherein the polynucleotide delivery system comprises the nucleic acid sequence of SEQ ID NO: 3.

32. The method of claim 27 wherein the hematopoietic stem cells are obtained from the patient.

33. The method of claim 27 wherein the hematopoietic stem cells are primary bone marrow cells.

34. A method of generating a T cell having specificity for a cancer cell comprising transfecting a hematopoietic stem cell with a recombinant retrovirus comprising a promoter linked to a polynucleotide encoding an  $\alpha$  subunit and a  $\beta$  subunit of a T cell receptor that is specific for an antigen present on the cancer cell.

35. The method of claim 34 wherein the polynucleotide comprises an IRES element disposed between the  $\alpha$  and  $\beta$  subunits of the T cell receptor.

36. The method of claim 34 wherein the polynucleotide additionally encodes a gene that enhances immune cell function.

37. A T cell that expresses a recombinant T cell receptor, wherein the recombinant T cell receptor is specific for a predetermined antigen and wherein the recombinant T cell receptor is the only T cell receptor expressed by the cell.

38. The T cell of claim 37 wherein the T cell receptor is specific for a cancer antigen.

39. The T cell of claim 38 wherein the T cell receptor is specific for a melanoma antigen.

40. The T cell of claim 37 wherein the T cell receptor is specific for a viral antigen.
41. The T cell of claim 40 wherein the T cell receptor is specific for an HIV antigen.
42. The T cell of claim 37 which expresses a gene that enhances T cell activity.